

**IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF DELAWARE**

MEDPOINTE HEALTHCARE INC.,

Plaintiff,

vs.

APOTEX INC. and APOTEX CORP.,

Defendants.

Civil Action No. 06-164-SLR

**CORRECTED PLAINTIFF'S REPLY TO DEFENDANTS'  
COUNTERCLAIMS TO AMENDED COMPLAINT**

Plaintiff MedPointe Healthcare Inc. ("MedPointe"), for its Reply to the counterclaims of Defendants Apotex Inc. and Apotex Corp. (collectively, "Apotex"), hereby states as follows:

**COUNTERCLAIM PARAGRAPH 35**

Apotex Inc. and Apotex Corp. adopt by reference, repeat, and reallege their specific responses and averments in paragraphs 1-26 above as though fully set forth herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 35**

MedPointe states that no reply is necessary to Paragraphs 1-26 of the Answer of Apotex Inc. and Apotex Corp. to Plaintiff's Amended Complaint, Affirmative Defenses and Counterclaims ("Apotex's Answer"), which merely respond to the averments in MedPointe's Amended Complaint. To the extent a reply is necessary, MedPointe restates Paragraphs 1-27 of its Amended Complaint and denies any contrary averments in Apotex's Answer. To the extent that Counterclaim Paragraph 35 contains any other or additional averments, MedPointe denies those averments.

**COUNTERCLAIM PARAGRAPH 36**

MedPointe has alleged that MedPointe Healthcare Inc. ("MedPointe") is a Delaware corporation having a place of business at 265 Davidson Avenue, Somerset, New Jersey 08873.

**REPLY TO COUNTERCLAIM PARAGRAPH 36**

Admitted.

**COUNTERCLAIM PARAGRAPH 37**

Apotex, Inc. is a Canadian corporation having a place of business at 150 Signet Drive, Weston, Ontario, Canada M9L 1 T9.

**REPLY TO COUNTERCLAIM PARAGRAPH 37**

Upon information and belief, MedPointe admits that Apotex Inc. is a Canadian corporation and that Apotex Inc. has a place of business at 150 Signet Drive, Weston, Ontario, Canada M9L 1T9.

**COUNTERCLAIM PARAGRAPH 38**

Apotex Corp. is a Delaware corporation having a place of business at 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326.

**REPLY TO COUNTERCLAIM PARAGRAPH 38**

Upon information and belief, MedPointe admits that Apotex Corp. is a Delaware corporation and that Apotex Corp. has a place of business at 2400 North Commerce Parkway, Suite 400, Weston, FL 33326.

**COUNTERCLAIM PARAGRAPH 39**

MedPointe manufactures and sells a pharmaceutical product under the trade name Astelin<sup>®</sup> that is a solution of azelastine hydrochloride for intranasal administration.

**REPLY TO COUNTERCLAIM PARAGRAPH 39**

MedPointe admits that it manufactures and sells Astelin<sup>®</sup> (azelastine hydrochloride) Nasal Spray, an antihistamine formulated as a metered-spray solution for intranasal administration. To the extent that Counterclaim Paragraph 39 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 40**

MedPointe was formed in 2001 when the healthcare division of Carter-Wallace was sold. One of the products included in the portfolio that became MedPointe was azelastine nasal spray.

**REPLY TO COUNTERCLAIM PARAGRAPH 40**

MedPointe admits that in 2001 Astelin<sup>®</sup> (azelastine hydrochloride) Nasal Spray was in the product portfolio of Wallace Laboratories, the healthcare division of Carter-Wallace, Inc. MedPointe further admits that in 2001 Carter-Wallace, Inc. changed its name to MedPointe

Healthcare Inc. To the extent that Counterclaim Paragraph 40 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 41**

MedPointe obtained approval from the Food and Drug Administration ("FDA") to market its Astelin<sup>®</sup> product pursuant to a New Drug Application ("NDA") 20-114 submitted by Carter-Wallace.

**REPLY TO COUNTERCLAIM PARAGRAPH 41**

MedPointe admits that the Wallace Laboratories division of Carter-Wallace, Inc. submitted New Drug Application ("NDA") 20-114 to the Food and Drug Administration ("FDA") and that the FDA approved NDA 20-114 on November 1, 1996. MedPointe further admits that it has approval from the FDA to market Astelin<sup>®</sup> (azelastine hydrochloride) Nasal Spray under NDA 20-114. To the extent that Counterclaim Paragraph 41 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 42**

MedPointe has represented to the FDA that the '194 patent claims the use of the drug azelastine as a nasal spray.

**REPLY TO COUNTERCLAIM PARAGRAPH 42**

MedPointe admits that, in accordance with applicable law, information regarding U.S. Patent No. 5,164,194 ("the '194 patent") was submitted to the FDA in connection with NDA 20-114 for Astelin<sup>®</sup> (azelastine hydrochloride) Nasal Spray. To the extent that Counterclaim Paragraph 42 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 43**

Relying in part on NDA 20-114, Apotex Inc. has submitted an Abbreviated New Drug Application ("ANDA") No. 77-954 for a proposed drug product containing azelastine hydrochloride for intra-nasal administration.

**REPLY TO COUNTERCLAIM PARAGRAPH 43**

Upon information and belief, MedPointe admits that on or about November 14, 2005, Apotex submitted ANDA 77-954 to the FDA under § 505(j) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355(j)). Upon information and belief, MedPointe admits that ANDA 77-954 seeks the FDA approval necessary to engage in the commercial manufacture, use, offer for sale and sale of a generic nasal spray product containing 0.1% azelastine hydrochloride in an aqueous solution for use in treating, *inter alia*, seasonal allergic rhinitis. To the extent that Counterclaim Paragraph 43 contains any other or additional averments, MedPointe is without knowledge or information sufficient to form a belief as to the truth of those averments and therefore denies them.

**COUNTERCLAIM PARAGRAPH 44**

Pursuant to 21 U.S.C. § 355(j)(2)(A)(vii) and 21 C.F.R. § 314.95, Apotex Inc. and Apotex Corp. have certified to MedPointe that the '194 patent is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of the new drug for which ANDA 77-954 is submitted.

**REPLY TO COUNTERCLAIM PARAGRAPH 44**

Upon information and belief, MedPointe admits that ANDA 77-954 contains an allegation under § 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355(j)(2)(A)(vii)(IV)) that the claims of the '194 patent are either invalid, unenforceable and/or will not be infringed by the manufacture, use or sale of the generic drug product for which ANDA 77-954 was submitted. MedPointe further admits that, as required by 21 C.F.R. § 314.95, Apotex provided MedPointe with written notification of ANDA 77-954 and its

§ 505(j)(2)(A)(vii)(IV) allegation. To the extent that Counterclaim Paragraph 44 contains any other or additional averments, MedPointe is without knowledge or information sufficient to form a belief as to the truth of those averments and therefore denies them.

**COUNTERCLAIM PARAGRAPH 45**

MedPointe has commenced this civil action against Apotex Inc. and Apotex Corp. alleging patent infringement.

**REPLY TO COUNTERCLAIM PARAGRAPH 45**

MedPointe admits that it commenced this action against Apotex Inc. and Apotex Corp. and that its Amended Complaint alleges infringement of the '194 patent. To the extent that Counterclaim Paragraph 45 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 46**

This case arises under the Constitution, laws, or treaties of the United States, viz., 35 U.S.C. §§ 1-376, which is an Act of Congress relating to patents, and 21 U.S.C. 355, which provide subject matter jurisdiction under 28 U.S.C. §§ 1331, 1338(a).

**REPLY TO COUNTERCLAIM PARAGRAPH 46**

MedPointe admits that Apotex purports to state declaratory judgment counterclaims that arise under 28 U.S.C. §§ 2201 and 2202 and the Patent Laws of the United States, 35 U.S.C. § 1, *et seq.* MedPointe further admits that this Court has subject matter jurisdiction over these counterclaims pursuant to 28 U.S.C. §§ 1331 and 1338(a). MedPointe, however, denies that there is any factual or legal basis for these counterclaims. To the extent that Counterclaim Paragraph 46 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 47**

A real, actual, and justiciable controversy exists between Apotex Inc. and Apotex Corp. on the one hand and MedPointe on the other hand regarding the invalidity of the '194 patent and Apotex' non-infringement thereof, constituting a case of actual controversy within the jurisdiction of this Court under the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202 (2005).

**REPLY TO COUNTERCLAIM PARAGRAPH 47**

MedPointe admits that Apotex, by infringing the '194 patent, has created an actual and justiciable controversy between itself and MedPointe regarding that infringement.

MedPointe further admits that Apotex purports to state declaratory judgment counterclaims that arise under 28 U.S.C. §§ 2201 and 2202 and the Patent Laws of the United States, 35 U.S.C. § 1, *et seq.* MedPointe, however, denies that there is any factual or legal basis for these counterclaims. To the extent that Counterclaim Paragraph 47 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 48**

Apotex Inc. and Apotex Corp. adopt by reference, repeat, and reallege their specific responses and averments in paragraphs 1-47 above as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 48**

MedPointe states that no reply is necessary to Paragraphs 1-27 of Apotex's Answer, which merely respond to the averments in MedPointe's Amended Complaint. To the extent a reply is necessary, MedPointe restates Paragraphs 1-27 of its Amended Complaint and denies any contrary averments in Apotex's Answer. MedPointe further states that no reply is necessary to Paragraphs 28-34 of Apotex's Answer, which merely purport to allege affirmative defenses on behalf of Apotex. To the extent a reply is necessary, MedPointe states as follows:

28. The '194 patent is invalid and/or unenforceable on grounds specified in United States Code, Title 35, including failure to comply with one or more of the requirements of 35 U.S.C. §§ 101, 102, 103, and/or 112.

**REPLY:** Denied.

29. The '194 patent is invalid under 35 U.S.C. § 102 over prior art including, but not limited to, United States Patents No. 3,813,384 and 4,704,387.

**REPLY:** Denied.

30. The '194 patent is invalid under 35 U.S.C. § 103 over prior art including, but not limited to, United States Patents No. 3,813,384, 4,704,387, 3,878,217, 4,254,129, 4,313,931, 4,430,343, Pecoud, A., et al., *International Archives of Allergy and Applied Immunology* (1987), Vol. 82, pp 541-543, Feinberg, S. M., *Transactions American Academy of Ophthalmology and Otolaryngology* (1950) Vol. 124, pp. 283-286, Pipkorn, U., et al., *Allergy* (1985) Vol. 40, pp. 491-496, Vanden Bussche, G., *Drugs of the Future* (1986) Vol. 11, pp. 841-843, Bende, M., et al., *Allergy* (1987), Vol. 42, pp. 512-515, Diamantis, W., et al., *Pharmacologist* (1981) Vol. 23, p. 149, Diamantis, W., et al., *Pharmacologist* (1982) Vol. 24, p. 200 (abstract no. 82 574 presented at ASPET meeting Louisville Kentucky, Aug 15-19 1982), and Kubo, N. et al., *Jpn. J. Pharmacol.* (1987) Vol. 43, pp. 277-82. The '194 patent is obvious in view of these references either individually, in combination with the knowledge of the person having ordinary skill in the art, or in combination with each other.

**REPLY:** Denied.

31. The '194 patent is unenforceable as procured through inequitable conduct. In violation of their duty of candor to the United States Patent & Trademark Office ("PTO"), applicants for the '194 patent misled the PTO about the properties of the alleged invention claimed therein. More particularly, circumstances constituting the applicants' inequitable conduct include, but are not limited to affirmative misrepresentation regarding the benefits of azelastine administered as a nasal spray.

**REPLY:** Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe denies each and every averment in Answer Paragraph 31.



32. The '194 patent asserts that the surprising feature of the invention is that the azelastine formulations of the '194 patent cause neither somnolence nor the bitter taste side effects of previous azelastine formulations. However, bitter taste is a well known side-effect of azelastine intranasal spray, as disclosed in, for example, *Curr. Med. Res. Opin.* (1997), Volume 14, No. 1, pp 21. MedPointe admits in its product insert for Astelin<sup>®</sup> brand azelastine nasal spray (attached as Exhibit A) indicates that major side effects include bitter taste (19.7% of individuals), somnolence (11.5% of individuals) and fatigue (2.3% of individuals).

**REPLY:** Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe responds as follows: MedPointe admits that the '194 patent states:

Surprisingly, in addition, none of the tiredness that arises with other applications was observed with use according to the invention.

Furthermore the invention provides a way to overcome problems which arise because of azelastine's exceptionally penetrating, bitter taste. The degree of the bitter taste is so intense that it is even found to be unpleasant in a dilution of 1 : 706. This problem has hitherto prevented oral application of azelastine solutions, since patients refuse to take such azelastine solutions or suspensions. It wa[s] surprisingly found in trial subjects that this bitter taste was no longer in evidence when the azelastine formulations of the invention were sprayed into the nose. As a result, it is possible in this manner to apply solutions or suspensions of azelastine and its salts nasally without taste impairment. Moreover the bitter taste is barely perceptible when the sprayed azelastine solution or suspension runs down into the pharynx.

(U.S. Patent No. 5,164,194, col. 1, l. 53 – col. 2, l. 2.) MedPointe further admits that the statements in *Curr. Med. Res. Opin.* (1997), Volume 14, No. 1, pp. 21, and the statements in the Astelin<sup>®</sup> Nasal Spray document attached as Exhibit A to Apotex's Answer speak for themselves. To the extent that Answer Paragraph 32 contains any other or additional averments, MedPointe denies them.

33. Also, during prosecution, the applicants argued, as an indicium of non-obviousness, that azelastine more effectively inhibited liberation of histamine compared with the prior art, the compound of Example 1 of United States Patent No. 4,704,387 even though Example 4 was closer to azelastine. A reasonable opportunity for further investigation or discovery is likely to provide evidentiary support and further evidentiary support that such acts were done with the intent to mislead the PTO and to fraudulently extend patent protection of azelastine.

**REPLY:** Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe responds as follows: MedPointe admits that during prosecution of the '194 patent a request for reconsideration dated December 26, 1989 was filed, which stated, *inter alia*:

Engel et al [U.S. Patent No. 4,704,387] discloses compounds whose structures are similar to that of the presently claimed azelastine, differing in the R group. In the Engel patent, R is benzyl, phenethyl, methoxyethyl or allyl, whereas, in the present invention, the corresponding group is methyl.

\* \* \*

While the process of applicant's claims 1-12 may be prima facie obvious, that process is not obvious because it produces an unobvious result. Applicants have conducted comparative experiments which demonstrate this advantage.

\* \* \*

The experiments are based on the fact that an allergic reaction in the eyes or the nose results from the liberation of histamine from mast cells as a result of the action of an antigen. The liberated histamine causes rhinitis symptoms.

\* \* \*

In the case of azelastine, the inhibition was 47.1% whereas, in the case of the compound 1 of Example 1 of the cited Engel patent, the inhibition was only 24.4%.

Thus, azelastine was about twice as effective as the compound of Example 1 of the Engel patent. This result is surprising and unexpected.

For this reason, it is submitted that the claimed process is unobvious.

MedPointe further admits that two declarations relating to these experiments were subsequently submitted to the PTO. To the extent that Answer Paragraph 33 contains any other or additional averments, MedPointe denies them.

34. The '194 patent is invalid and obtained fraudulently and by inequitable conduct. MedPointe submitted the '194 patent to the FDA to be listed among Approved Drug Products With Therapeutic Equivalence Evaluation (also known as the "Orange Book") as covering azelastine hydrochloride. MedPointe also has commenced this infringement action against Apotex. MedPointe's efforts to enforce the '194 patent, by infringement suits and by listing that patent in the Orange Book, constitute patent misuse.

**REPLY:** Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe responds as follows: MedPointe admits that, in accordance with applicable law, information regarding U.S. Patent No. 5,164,194 ("the '194 patent") was submitted to the FDA for listing in the Orange Book in connection with Astelin<sup>®</sup> (azelastine hydrochloride) Nasal Spray. MedPointe also admits that it brought this patent infringement suit against Apotex. To the extent that Answer Paragraph 34 contains any other or additional averments, MedPointe denies them.

MedPointe further restates its responses to Counterclaim Paragraphs 35-47 as though fully set forth herein. To the extent that Counterclaim Paragraph 48 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 49**

The '194 patent is invalid and/or unenforceable on grounds specified in United States Code, Title 35, including failure to comply with one or more of the requirements of 35 U.S.C. §§ 101, 102, 103, and/or 112.

**REPLY TO COUNTERCLAIM PARAGRAPH 49**

Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe denies each and every averment in Counterclaim Paragraph 49.

**COUNTERCLAIM PARAGRAPH 50**

Apotex Inc. and Apotex Corp. adopt by reference, repeat, and reallege its specific responses and averments in paragraphs 1-49 above as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 50**

MedPointe states that no reply is necessary to Paragraphs 1-27 of Apotex's Answer, which merely respond to the averments in MedPointe's Amended Complaint. To the extent a reply is necessary, MedPointe restates Paragraphs 1-27 of its Amended Complaint and denies any contrary averments in Apotex's Answer. MedPointe further states that no reply is necessary to Paragraphs 28-34 of Apotex's Answer, which merely purport to allege affirmative defenses on behalf of Apotex. To the extent a reply is necessary, MedPointe restates its responses to Answer Paragraphs 28-34, as set forth above in MedPointe's Reply to Counterclaim Paragraph 48, as though fully set forth herein. MedPointe further restates its responses to Counterclaim Paragraphs 35-49 as though fully set forth herein. To the extent that Counterclaim Paragraph 50 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 51**

The '194 patent issued Nov. 17, 1992 from Patent Application number 07/551,644 filed July 12, 1990, which purported to be a continuation of Patent Application number 07/268,772, filed November 9, 1988 and subsequently abandoned, and purports to claim priority from the German Patent Application number 373681 filed Nov. 13, 1987.

**REPLY TO COUNTERCLAIM PARAGRAPH 51**

MedPointe admits that the '194 patent issued on November 17, 1992 from patent application serial number 07/551,644 filed on July 12, 1990, which was a continuation of patent application serial number 07/268,772 filed on November 9, 1988 and subsequently abandoned, and claims priority from German patent application number 3738681 filed on November 13, 1987. To the extent that Counterclaim Paragraph 51 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 52**

United States Patent No. 3,813,384 is prior art with regard to the '194 patent under one or more of the provisions of 35 U.S.C. § 102.

**REPLY TO COUNTERCLAIM PARAGRAPH 52**

MedPointe admits that United States Patent No. 3,813,384 bears on its face an issue date that is prior to the filing date of the earliest application to which the '194 patent claims priority, German patent application number 3738681 filed on November 13, 1987. To the extent that Counterclaim Paragraph 52 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 53**

United States Patent No. 4,704,387 are *[sic]* prior art with regard to the '194 patent under one or more of the provisions of 35 U.S.C. § 102.

**REPLY TO COUNTERCLAIM PARAGRAPH 53**

MedPointe admits that United States Patent No. 4,704,387 bears on its face an issue date that is prior to the filing date of the earliest application to which the '194 patent claims priority, German patent application number 3738681 filed on November 13, 1987. To the extent that Counterclaim Paragraph 53 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 54**

The '194 patent is invalid under 35 U.S.C. § 102 over prior art including, but not limited to, the prior art listed in ¶¶ 54-55 *[sic]* above.

**REPLY TO COUNTERCLAIM PARAGRAPH 54**

Denied.

**COUNTERCLAIM PARAGRAPH 55**

Apotex Inc. and Apotex Corp. adopt by reference, repeat, and reallege their specific responses and averments in paragraphs 1-54 above as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 55**

MedPointe states that no reply is necessary to Paragraphs 1-27 of Apotex's Answer, which merely respond to the averments in MedPointe's Amended Complaint. To the extent a reply is necessary, MedPointe restates Paragraphs 1-27 of its Amended Complaint and denies any contrary averments in Apotex's Answer. MedPointe further states that no reply is necessary to Paragraphs 28-34 of Apotex's Answer, which merely purport to allege affirmative defenses on behalf of Apotex. To the extent a reply is necessary, MedPointe restates its

responses to Answer Paragraphs 28-34, as set forth above in MedPointe's Reply to Counterclaim Paragraph 48, as though fully set forth herein. MedPointe further restates its responses to Counterclaim Paragraphs 35-54 as though fully set forth herein. To the extent that Counterclaim Paragraph 55 contains any other or additional averments, MedPointe denies them.

#### **COUNTERCLAIM PARAGRAPH 56**

The scope and content of the prior art includes, but is not limited to, United States Patents No. 3,813,384, 4,704,387, 3,878,217, 4,254,129, 4,313,931, 4,430,343, Pecoud, A., et al., *International Archives of Allergy and Applied Immunology* (1987), Vol. 82, pp. 541-543, Feinberg, S. M., *Transactions American Academy of Ophthalmology and Otolaryngology* (1950) Vol. 124, pp. 283-286, Pipkorn, U., et al., *Allergy* (1985) Vol. 40, pp. 491-496, Vanden Bussche, G., *Drugs of the Future* (1986) Vol. 11, pp. 841-843, Bende, M., et al., *Allergy* (1987), Vol. 42, pp. 512-515, Diamantis W, et al., *Pharmacologist* (1981) Vol. 23, p. 149, Diamantis W, et al., *Pharmacologist* (1982) Vol. 24, pp. 200, and Kubo N et al., *Jpn. J. Pharmacol.* (1987) Vol. 43, pp. 277-82. The '194 patent is obvious in view of these references either individually, in combination with the knowledge of the person having ordinary skill in the art, or in combination with each other.

#### **REPLY TO COUNTERCLAIM PARAGRAPH 56**

MedPointe admits that United States Patents No. 3,813,384, 4,704,387, 3,878,217, 4,254,129, 4,313,931, 4,430,343 bear on their face issue dates that are prior to the filing date of the earliest application to which the '194 patent claims priority, German patent application number 3738681 filed on November 13, 1987. MedPointe also admits that Feinberg, S. M., *Transactions American Academy of Ophthalmology and Otolaryngology* (1950) Vol. 124, pp. 283-286, Pipkorn, U., et al., *Allergy* (1985) Vol. 40, pp. 491-496, Vanden Bussche, G., *Drugs of the Future* (1986) Vol. 11, pp. 841-843, Diamantis W, et al., *Pharmacologist* (1981) Vol. 23, p. 149 and Diamantis W, et al., *Pharmacologist* (1982) Vol. 24, pp. 200 are dated on their face before the earliest application to which the '194 patent claims priority. MedPointe further admits that Pecoud, A., et al., *International Archives of Allergy and Applied Immunology* (1987), Vol. 82, pp. 541-543, Bende, M., et al., *Allergy* (1987), Vol. 42, pp. 512-515 and Kubo N

et al., *Jpn. J. Pharmacol.* (1987) Vol. 43, pp. 277-82 are dated on their face in 1987. To the extent that Counterclaim Paragraph 56 contains any other or additional averments, MedPointe denies them.

**COUNTERCLAIM PARAGRAPH 57**

The differences between the subject matter claimed in the '194 patent and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

**REPLY TO COUNTERCLAIM PARAGRAPH 57**

Denied.

**COUNTERCLAIM PARAGRAPH 58**

Apotex Inc. and Apotex Corp. adopt by reference, repeat, and reallege their specific responses and averments in paragraphs 1-57 above as though set forth fully herein.

**REPLY TO COUNTERCLAIM PARAGRAPH 58**

MedPointe states that no reply is necessary to Paragraphs 1-27 of Apotex's Answer, which merely respond to the averments in MedPointe's Amended Complaint. To the extent a reply is necessary, MedPointe restates Paragraphs 1-27 of its Amended Complaint and denies any contrary averments in Apotex's Answer. MedPointe further states that no reply is necessary to Paragraphs 28-34 of Apotex's Answer, which merely purport to allege affirmative defenses on behalf of Apotex. To the extent a reply is necessary, MedPointe restates its responses to Answer Paragraphs 28-34, as set forth above in MedPointe's Reply to Counterclaim Paragraph 48, as though fully set forth herein. MedPointe further restates its responses to Counterclaim Paragraphs 35-57 as though fully set forth herein. To the extent that Counterclaim Paragraph 58 contains any other or additional averments, MedPointe denies them.



**COUNTERCLAIM PARAGRAPH 59**

In violation of their duty of candor to the United States Patent & Trademark Office ("PTO"), applicants for the '194 patent misled the PTO about the properties of the alleged invention claimed therein. More particularly, circumstances constituting the applicants' inequitable conduct include, but are not limited to affirmative misrepresentation regarding the benefits of azelastine administered as a nasal spray.

**REPLY TO COUNTERCLAIM PARAGRAPH 59**

Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe denies each and every averment in Counterclaim Paragraph 59.

**COUNTERCLAIM PARAGRAPH 60**

The '194 patent asserts that the surprising feature of the invention is that the azelastine formulations of the '194 patent cause neither somnolence nor the bitter taste side effects of previous azelastine formulations. However, bitter taste is a well known and common effect of azelastine nasal spray administration, as disclosed in, for example, *Curr. Med. Res. Opin.* (1997), Volume 14, No. 1, pp. 21. MedPointe admits in its product insert for Astelin<sup>®</sup> brand azelastine nasal spray (attached as Exhibit A) indicates that major side effects include bitter taste (19.7% of individuals), somnolence (11.5% of individuals) and fatigue (2.3% of individuals).

**REPLY TO COUNTERCLAIM PARAGRAPH 60**

Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe responds as follows: MedPointe admits that the '194 patent states:

Surprisingly, in addition, none of the tiredness that arises with other applications was observed with use according to the invention.

Furthermore the invention provides a way to overcome problems which arise because of azelastine's exceptionally penetrating, bitter taste. The degree of the bitter taste is so intense that it is even found to be unpleasant in a dilution of 1 : 706. This problem has hitherto prevented oral application of azelastine solutions, since patients refuse to take such azelastine solutions or suspensions. It

wa[s] surprisingly found in trial subjects that this bitter taste was no longer in evidence when the azelastine formulations of the invention were sprayed into the nose. As a result, it is possible in this manner to apply solutions or suspensions of azelastine and its salts nasally without taste impairment. Moreover the bitter taste is barely perceptible when the sprayed azelastine solution or suspension runs down into the pharynx.

(U.S. Patent No. 5,164,194, col. 1, l. 53 – col. 2, l. 2.) MedPointe further admits that the statements in *Curr. Med. Res. Opin.* (1997), Volume 14, No. 1, pp. 21, and the statements in the Astelin<sup>®</sup> Nasal Spray document attached as Exhibit A to Apotex's Answer speak for themselves. To the extent that Counterclaim Paragraph 60 contains any other or additional averments, MedPointe denies them.

#### **COUNTERCLAIM PARAGRAPH 61**

Also, during prosecution, the applicants argued, as an indicium of non-obviousness, that azelastine more effectively inhibited liberation of histamine compared with the prior art, the compound of Example 1 of United States Patent No. 4,704,387 even though Example 4 was closer to azelastine. A reasonable opportunity for further investigation or discovery is likely to provide evidentiary support and further evidentiary support that such acts were done with the intent to mislead the PTO and to fraudulently extend patent protection of azelastine.

#### **REPLY TO COUNTERCLAIM PARAGRAPH 61**

Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe responds as follows: MedPointe admits that during prosecution of the '194 patent a request for reconsideration dated December 26, 1989 was filed, which stated, *inter alia*:

Engel et al [U.S. Patent No. 4,704,387] discloses compounds whose structures are similar to that of the presently claimed azelastine, differing in the R group. In the Engel patent, R is benzyl, phenethyl, methoxyethyl or allyl, whereas, in the present invention, the corresponding group is methyl.

\* \* \*

While the process of applicant's claims 1-12 may be prima facie obvious, that process is not obvious because it produces an unobvious result. Applicants have conducted comparative experiments which demonstrate this advantage.

\* \* \*

The experiments are based on the fact that an allergic reaction in the eyes or the nose results from the liberation of histamine from mast cells as a result of the action of an antigen. The liberated histamine causes rhinitis symptoms.

\* \* \*

In the case of azelastine, the inhibition was 47.1% whereas, in the case of the compound 1 of Example 1 of the cited Engel patent, the inhibition was only 24.4%.

Thus, azelastine was about twice as effective as the compound of Example 1 of the Engel patent. This result is surprising and unexpected.

For this reason, it is submitted that the claimed process is unobvious.

MedPointe further admits that two declarations relating to these experiments were subsequently submitted to the PTO. To the extent that Counterclaim Paragraph 61 contains any other or additional averments, MedPointe denies them.

#### **COUNTERCLAIM PARAGRAPH 62**

A reasonable opportunity for further investigation or discovery is likely to provide evidentiary support and further evidentiary support that the foregoing misrepresentations and failure to disclose material prior art as set forth above were done with intent to mislead the PTO.

#### **REPLY TO COUNTERCLAIM PARAGRAPH 62**

Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe denies each and every averment in Counterclaim Paragraph 62.

**COUNTERCLAIM PARAGRAPH 63**

The facts and circumstances set forth in this Count IV constitute inequitable conduct on the part of Applicants, making the '194 patent unenforceable.

**REPLY TO COUNTERCLAIM PARAGRAPH 63**

Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe denies each and every averment in Counterclaim Paragraph 63.

**COUNTERCLAIM PARAGRAPH 64**

A reasonable opportunity for further investigation or discovery is likely to provide evidentiary support for other and further circumstances constituting inequitable conduct by the applicants.

**REPLY TO COUNTERCLAIM PARAGRAPH 64**

Subject to Plaintiff's Motion to Strike Apotex's Jury Demand, Strike Apotex's Affirmative Defense of Unenforceability, Dismiss Apotex's Counterclaim of Unenforceability, and Strike Apotex's Affirmative Defense of Misuse, filed concurrently herewith, MedPointe denies each and every averment in Counterclaim Paragraph 64.

**COUNTERCLAIM DEMAND FOR JUDGMENT AND PRAYER FOR RELIEF**

WHEREFORE, Apotex Inc. and Apotex Corp. pray for judgment:

- A. Finding that the '194 patent is invalid and unenforceable;
- B. Finding that the '194 patent is not infringed;
- C. Finding that this is an exceptional case under 35 U.S.C. § 285;
- D. Awarding to Apotex Inc. and Apotex Corp. its costs, expenses, and reasonable attorneys' fees and other relief the Court deems just.

**REPLY TO COUNTERCLAIM DEMAND FOR JUDGMENT  
AND PRAYER FOR RELIEF**

MedPointe denies that Apotex is entitled to any relief whatsoever from MedPointe or the Court, either as prayed for in its Counterclaims or otherwise.

MedPointe also denies that Apotex is entitled to litigate non-infringement of the '194 patent, as non-infringement was not pled either as an affirmative defense or counterclaim.

MedPointe further denies each and every allegation contained in Apotex's Answer and Counterclaims that was not specifically admitted, denied or otherwise responded to in this Reply.

**COUNTERCLAIM DEMAND FOR JURY TRIAL**

Apotex Inc. and Apotex Corp. demand trial by jury for all issues triable by jury as a matter of right.

**REPLY TO DEMAND FOR JURY TRIAL**

MedPointe denies that Apotex is entitled to a jury trial. MedPointe further denies that there are any issues in this action that are triable by jury as a matter of right.

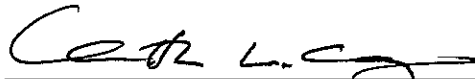
**MEDPOINTE'S PRAYER FOR RELIEF**

WHEREFORE, MedPointe prays for judgment as follows:

- A. Dismissing Apotex's Counterclaims with prejudice;
- B. Awarding MedPointe the relief sought in its Amended Complaint;
- C. Awarding MedPointe its costs, attorneys' fees and expenses incurred in this action; and
- D. Awarding MedPointe such further relief as the Court deems just and proper.

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Dated: May 5, 2006

*Attorneys for Plaintiff  
MedPointe Healthcare Inc.*

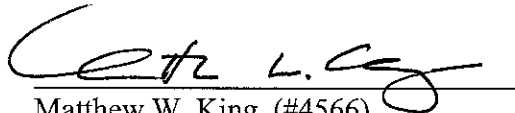
**CERTIFICATE OF SERVICE**

I HEREBY CERTIFY that on May 5, 2006, I electronically filed the foregoing document with the Clerk of Court using CM/ECF which will send notification of such filing, and hand delivered to the following:

Richard L. Horwitz, Esq.  
POTTER ANDERSON & CORROON LLP  
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1313 N. Market Street  
Wilmington, DE 19801

I HEREBY CERTIFY that on May 5, 2006, I sent the foregoing document by Federal Express, next business day delivery, to the following non-registered participant:

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